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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,332	05/21/2001	Thomas G. Burke	434-204	5935

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EXAMINER	
NGUYEN, DAVE TRONG	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,332	BURKE ET AL.	
	Examiner	Art Unit	
	Dave T Nguyen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *9-13, 15-21, 23-25* is/are allowed.

6)☒ Claim(s) *14 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 18, 2003 has been entered.

Claims 10 and 18 have been amended by the amendment dated December 18, 2003.

Claims 9-25 are pending for examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10, 15, 18 and 23 [24, which was a typographical error in the final stated rejection of record] remain rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's claims 10, 15, 18 and 23 embrace a viral vector such as an adenoviral vector, which contains within macromolecular assemblies, a CPT/oligo complex. Applicant's contemplates on page 25, for example, that the CPTs complexes can be introduced, stored and delivered in a stable manner while being bound in the active lactone form to the oligos contained in the viral vectors. Applicant neither provides any guidance nor working examples so as to enable a skilled artisan to reasonably prepare such viral vectors within the framework of the claimed invention.

The state of the art of using viral vectors to deliver DNA (Verma, Nature, Vol. 389, 1997, 239-242) is that the DNA has to be prepared in an expressible structure, which comprises a regulatory sequence operably linked to a coding sequence of a desire DNA such as an antisense mRNA. However, the as-filed specification teaches that any oligonucleotide/CPT can be stored and maintained in a viral vector, and yet, the as-filed specification does not provide any guidance as to how CPT which is a toxic drug can be stored stably in any viral vector to the extent that the intended use of the viral vectors containing CPT/oligo complexes can be achieved so as to have a chemotherapeutic effect. The issue is not whether or not an oligonucleotide sequence by itself can be prepared and by expressed by any known viral vector such as those as recited in claim 15. The issue is that the main thrust of the invention can be reasonably construed as a method of making and use a virally delivery vector, which can package, produce stably a complex composed of an oligoncuelotide complexed to a

chemotherapeutic drug such as CPT, and to secret the complex out into an outside environment in order to exert its therapeutic effect on a tumor cell. The only information that the as-filed specification relies upon for the making and use of such virally delivery vectors is the knowledge from a person skilled in the art. An extensive search of prior art does not reproduce any prior art that could teach a protocol of making and use a viral vector that could package, produce, and store a complex composed of any chemotherapeutic drug complexed to an oligonucleotide. Simple statements stating that existing recombinant DNA techniques are well-known in the prior art, and that a viral vector can package, deliver, and express a CPT/oligonculeotide complex are not the same as a sufficient guidance which is needed to make and use a viral vector that could package, deliver and express or secrete the CPT complex out into a target tissue containing target tumor cells. The state of the art with respect to the use of CPTs in a virus (Pantazis, J. Biomedical Science, 6, 1, 1-7, 1999) is that CPT is a potent inhibitor of replication, transcription and packaging of double-stranded DNA-containing adenoviruses, papovariruses and herpesviruses. As such, the only way that any CPT could be stored in a viral vector is that must remains complexed to an oligonucleotide in order to be stable and not toxic to the delivery viral vectors. If that is the case, it is not apparent as to how a skilled artisan, on the basis of existing DNA recombinant technique, to prepare a distinct entity of a complex composed of a chemical CPT drug complexed with an oligonucleotide in a viral vector, without resulting on an undue experimentation. The as-filed specification discloses that virally recombinant DNA protocols are available in the prior art. However, the DNA recombinant techniques only

provides sufficient guidance the making of an oligonucleotide sequence composed solely of nucleotide residues by a viral vector, wherein an expression cassette or box is a prerequisite for the making of the oligonucleotide. A complex composed of a CPT complexed to an oligonculeotide is not the same as a simple oligonucleotide. If a skilled artisan would not have been able to reasonably extrapolate from the making of a unmodified or uncomplexed oligonucleotide by a viral vector to the making of a viral vector containing and/or expressing a CPT/oligonucleotide complex, it would naturally flows from the *Wands factors* that it not apparent how a skilled artisan, without any undue experimentation, can prepare the claimed viral vectors so as to use within applicant's framework of the claimed invention, particularly in view of the reasons set forth above.

Applicant's response (pages 9-13, dated December 18, 2003) has been considered by the examiner but is not found persuasive for the reasons set forth in the above stated rejection, which have been further clarified on the basis of the previously stated rejection.

Applicant mainly argues that undue experimentation is not required, that working examples are not required to satisfy the enablement of the claimed invention, and that the knowledge available to a person of skill in the art and the disclosure of the claimed invention are sufficient to one of skill in the art to make and use the claimed invention, without undue experimentation, citing *In re Borkowski, Northern Telecom, Inc. v Datapoint Corp, MPEP 2164.03,* and *In re Wands.* However, the argument appears to be directed to the making and use of an uncomplexed oligonucleotide by a virally

delivery vector. However, such is not the issue as set forth in the stated rejection, nor is it the issue of toxicity caused by a CPT/oligonucleotide complex. As set forth and clarified in the above stated rejection, the issue is that the main thrust of the invention can be reasonably construed as a method of making and use a virally delivery vector, which can package, produce stably a complex composed of an oligoncuelotide complexed to a chemotherapeutic drug such as CPT, and to secret the complex out into an outside environment in order to exert its therapeutic effect on a tumor cell. The only information that the as-filed specification relies upon for the making and use of such virally delivery vector as clamed is the knowledge from a person skilled in the art. An extensive search of prior art does not reproduce any prior art that could teach a protocol of making and use a viral vector that could package, produce, and store a complex composed of any chemotherapeutic drug complexed to an oligonucleotide. Simple statements stating that existing recombinant DNA techniques are well-known in the prior art, and that a viral vector can package, deliver, and express a CPT/oligonculeotide complex are not the same as a sufficient guidance which is needed to make and use a viral vector that could package, deliver and express or secrete the CPT complex out into a target tissue containing target tumor cells. As such, until applicant's response could provide substantial evidence showing that the making and use of applicant's claimed virally delivery vector expressing or secreting a CPT/oligonucleotide complex is a routine experimentation, the stated rejection remains proper for the reasons of record.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 18-21 are rejected under 35 USC 102(a) as being anticipated by Thompson Strode, H. Peter Spielmann, and Andrew Wang, as co-authors of the reference cited in J. Am. Chem. Soc. 120, 2979-2980, Published on Web, March 12, 1998.

Thompson Strode, H. Peter Spielmann, and Andrew Wang (Strode) teaches that the hydrolysable alpha-hydroxy-lactone ring of any camptothecin used as a chemotherapeutic drug is essential for CPTs efficacy. In addition, Strode teaches that CTPs-duplex oligonucleotide complexes when prepared as a mixture of CPTs and

oligonucleotides in a typical PBS buffer, promotes the complex formation between CPTs and the oligonucleotides and stabilizes the lactone forms of CPT (page 361 bridging page 362, and page 363).

Absent evidence to the contrary, the composition discloses in Strode has all of the functional properties as recited in the claims.

Applicant mainly argues with respect to all of the prior art rejections employing Strode that the Strode reference is not a proper 102(a) reference because:

The Strode reference describes the Applicant's work; and the description of Applicant's work as set froth in the Strode reference is only described by the inventors of the present application, *e.g.,* Yang and Burke (now deceased).

Applicant argument is not found persuasive because as evidenced by the presence of the names of "others" who together with Burke and Yang describe the same invention as set forth in the rejected claims, the examiner maintains that Thompson Strode, H. Peter Spielmann, and Andrew H.J Wang would constitute as "others", which described applicant's claimed invention in a printed publication (dated March 12, 1998) before the effective filing date of the as-filed specification (dated October 14 1998). Thus, insofar as the Thompson Strode, H. Peter Spielmann, and Andrew H.J Wang are not applicants but rather "others" who describe the same invention as set forth in the rejected claims, the disclosure is therefore not applicant's own work, particularly in the absence of evidence to the contrary.

The examiner acknowledges that on the basis of MPEP 706.02(b),

A rejection based on 35 U.S.C. 102(a) can be overcome by:
(A) Persuasively arguing that the claims are patentably distinguishable from the prior art;
(B) Amending the claims to patentably distinguish over the prior art;
(C) Filing an affidavit or declaration under 37 CFR 1.131 showing prior invention, if the reference is not a U.S. patent or a U.S. patent application publication claiming the same patentable invention as defined in 37 CFR 1.601(n). See MPEP § 715 for information on the requirements of 37 CFR 1.131 affidavits. When the claims of the reference U.S. patent or U.S. patent application publication and the application are directed to the same invention or are obvious variants, an affidavit or declaration under 37 CFR 1.131 is not appropriate to overcome the rejection.<
(D) **Filing an affidavit or declaration under 37 CFR 1.132 showing that the reference invention is not by "another." See MPEP § 715.01(a), § 715.01(c), and § 716.10**;
(E) Perfecting a claim to priority under 35 U.S.C. 119(a)-(d) as explained in reference to 35 U.S.C. 102(e) above;
(F) Perfecting priority under 35 U.S.C. 119(e) or 120 **>as explained in reference to 35 U.S.C. 102(e) above.

Until item D, for example, is set forth in the record properly, the rejection remains proper and is maintained.

Claims 18-21 are rejected under 35 USC 102(b) as being anticipated by Chourpa (Specgtroscopy of Bviological Molecules: Modern Trends, [European Conferenceon Spectroscopy of Biological Molecules], 7th, Madrid, 1997, as evidenced by the as-filed specification, working examples and pages 8 and 9.

Chourpa teaches it is well recognized in the prior art that the hydrolysable alpha-hydroxy-lactone ring of any camptothecin used as a chemotherapeutic drug is essential for CPTs efficacy. In addition, Chourpa teaches that CTPs-oligonucleotide (ds oligo 1 or oligo 2/CPT) complexes when prepared as a mixture of CPTs and synthetic oligonucleotides in a typical aqueous buffer at PH 7.3, promotes the complexation

between CPTs and the oligonucleotides and stabilizes the lactone forms of CPT (page 361 bridging page 362, and page 363). The fact that a composition comprising oligo 1 or oligo 2 together with lactone camptothetcin drug is stable is indicative of a proper anticipation of the claimed composition, which clearly embraces any composition comprising any oligo in combination with a lactone camptothecin drug, and as such, the composition comprising oligo 1 or oligo 2 together with lactone camptothetcin drug anticipates the claimed composition. The presently rejected claims are in no way limited to a particular set of oligonucleotide (excluding sequences with topol cleavage sites, for example).

Also, not only the specification teaches and embraces a complex comprising a CPT and an oligonculeotide in any form or sequence structure, the as-filed specification also contemplates that CPT is complexed to oligos in a reversible manner when complexed in a non-covalent bond. On the basis of this evidence, there is no doubts that that the complex of the prior art cannot be uncomplexed during its traversal *in vivo* to a target tumor site, *e.g.,* oligo degradation due to nuclease attack, and natural uncouplings of the non-covalent bond.

Note that under MPEP guideline, a claim directed to an old product where a discovery of a new property or a new use of an old product is not patentable. In addition, MPEP 2114 indicates that "MANNER OF OPERATING THE DEVICE DOES NOT DIFFERENTIATE APPARATUS CLAIM FROM THE PRIOR ART".

Absent evidence to the contrary, the compositions discloses in Chourpa read on the broadly claimed invention, and have all of the functional properties as recited in the claims.

Applicant (the response pages 14-15) further attempts to rely upon the teaching of oligonculeotide 3 only in order to allege that Chourpa does not teach the claimed composition. However, the rejection is in no way meant to be focused on oligonucleotide 3. The fact that a composition comprising oligo 1 or oligo 2 together with lactone camptothetcin drug is taught in Chourpa is indicative of a proper anticipation of the claimed composition which clearly embraces any composition comprising any oligo in combination with a lactone camptothecin drug, and as such, the composition comprising oligo 1 or oligo 2 together with lactone camptothetcin drug is clearly embraced by the broad scope of the claimed invention, and thus, anticipates the claimed composition. Again, Applicant asserts the functional limitations as indicated above, however, there is no substantial evidence to show that the compositions of Chourpa does not exhibit either a therapeutic activity, or the ability to naturally release the oligo from the complex. In fact, as evidenced by the as-filed specification, not only the specification teaches and embraces a complex comprising a CPT and an oligonculeotide in any form or sequence structure, the as-filed specification also contemplates that CPT is complexed to oligos in a reversible manner. On the basis of this evidence, there is no doubts that that the complex of the prior art cannot be uncomplexed during its traversal *in vivo* to a target tumor site, *e.g.,* oligo degradation

due to nuclease attack, and natural uncouplings of the non-covalent bond. Furthermore, Chourpa teaches that it is well recognized in the prior art that the hydrolysable alpha-hydroxy-lactone ring of any camptothecin used as a chemotherapeutic drug is essential for CPTs efficacy. In addition, Chourpa teaches that CTPs-oligonucleotide complexes when prepared as a mixture of CPTs and synthetic oligonucleotides in a typical aqueous buffer at PH 7.3, promotes the complexation between CPTs and the oligonucleotides and stabilizes the lactone forms of CPT. As such, given the well-recognized use of hydrolysable alpha-hydroxy-lactone ring of any camptothecin used as a chemotherapeutic drug, it is apparent that the composition comprosomg a mixture of CPTs and synthetic oligonucleotides comprising GC base pairs in a typical aqueous buffer at PH 7.3, promotes the complexation between CPTs and the oligonucleotides and stabilizes the lactone forms of CPT, which would necessarily lead to its efficacy as a chemotherapeutic drug, particularly in the absence of evidence to the contrary, and in view of the reasons as discussed *suppra.*

As such, given that claim 18 remains properly rejected over the prior art, the citations of *Verdegaal Bros, v. Union Oil Co. of California,* are not found persuasive.

Claims 9-13, 18-21 are rejected under 35 USC 103(a) as being unpatentable over Green et al. (US Pat No. 5,583,034) taken with either Strode or Chourpa (Specgtroscopy of Bviological Molecules: Modern Trends, [European Conferenceon Spectroscopy of Biological Molecules], 7th, Madrid, 1997, 361-362 alone. Note that this rejection has been modified to clarify the issues of record.

Green teaches a pharmaceutical composition for treating a tumor, wherein the pharmaceutical composition comprising a mixture of Camptothecins (CPTs) in a pharmaceutically acceptable buffer and/or carrier (column 8, lines 16-26, column 9, lines 11-24). Column 6, lines 36-66 of Green also discloses that liposomal carrier can be used to encapsulate and deliver the antisense oligonucleotide composition, and that any pharmaceutically acceptable buffer or aqueous solution can be used to prepare the antisense oligonucleotide composition. In addition, columns 11 and 12 disclose the sequence structure of the antisense oligos comprising **GC base pairs.**

Green does not teach that lactone forms must be present in a Camptothecin, and that the antisense oligos are complexed to CPT in the pharmaceutical composition.

However, at the time the invention was made, it is well known in the prior art that (as evidenced by Chourpa and Strode), that the hydrolysable alpha-hydroxy-lactone ring of any camptothecin used as a chemotherapeutic drug in cancer treatments is essential for CPTs efficacy. In addition, Chourpa and Strode both teach that CTPs-oligonucleotide complexes when prepared as a complex of CPTs and double stranded oligonucleotides containing a string of GC base pairs or and AT base pairs, respectively, in a typical aqueous buffer, promotes the complexation between CPTs and the oligonucleotides and stabilizes the lactone forms of CPT.

It would have been obvious for one of ordinary skill in the art to employed the pure lactone forms of CPTs stabilized by either a double stranded oligo or nucleic acid molecules comprising either AT base pairs or GC base pairs as the chemotherapeutic drug in the pharmaceutical composition of Green. One would have been motivated to

complex a CTP to a double stranded oligo composed of either GC base pairs or AT base pairs, because is well-known in the prior art, as exemplified by Chourpa and Strode, that the hydrolysable alpha-hydroxy-lactone ring of any camptothecin stabilized by a AT based double stranded oligo or GC based double stranded oligo is essential for CPTs efficacy.

It would also have been obvious for one of ordinary skill in the art to employ a combination of a CPT and an antisense molecule as disclosed on columns 11 and 12 of Green so as to enhance a combination effect in tumor treatments, particularly in light of the teachings of combined references as set forth above. As such, it would have been obvious to one of ordinary skill in the art that the affinity between CPTs and antisense oligonucleotides composed of GC base pairs as disclosed on columns 11 and 12 of Green, so as to form a complex of CPTs and oligos is the intrinsic property of the CPTs when put in contact with oligonucleotides, particularly in light of the both Strode and Chourpa references, which teach that as long as a mixture of CPTs and GC oligos is prepared in a typical buffer solution, complexes of CPTs and oligos are formed as a result of the affinity.

Thus, the claimed invention as a whole was prima facie obvious.

Claims 10, 16-18, 24, 25 are rejected under 35 USC 103(a) as being unpatentable over Green et al. (US Pat No. 5,583,034) taken with either Strode or Chourpa (Specgtroscopy of Bviological Molecules: Modern Trends, [European

Conferenceon Spectroscopy of Biological Molecules], 7th, Madrid, 1997, 361-362, and further in view of Perez-Soler et al. (US Pat No. 5,834,012).

Green taken with either Strode or Chourpa is applied here as indicated above.

While Green teaches that liposomal carriers can be used to deliver therapeutic agents such as antisense molecules, Green taken with Strode or Chourpa does not teach as a whole that the CPT complex can be trapped or delivered by a lipid based carrier such as a liposome. However, Perez-Soler et al. teaches that CPTs drugs are well described in the prior art and that liposomes can be used to trap and stabilize the lactone form of CPT (entire disclosure, particularly column 1 bridging column 2, and column 3).

it would have been obvious for one of ordinary skill in the art to have employed any known liposomal carrier or lipid based carrier to deliver the antisense oligo/CPT complexes present in the pharmaceutical composition of Green taken with Chourpa. One would have been motivated to do so because column 6, lines 36-66 of Green also discloses that liposomal carrier can be used to encapsulate and deliver the antisense oligonucleotide composition, and/or because Perez-Soler et al. teaches that CPTs drugs are well-described in the prior art and that liposomes can be used to stabilize the lactone form of CPT.

Thus, the claimed invention as a whole was prima facie obvious.

Applicant's argument (pages 16-17) directed to the 103 rejection is essentially the same as that for the 102 rejections based on either Strode or Chourpa, and is not found persuasive because of the reasons as discussed *suppra.*

The rejections of Claims 10, 14, 18 and 22 under 35 USC 103(a) as being unpatentable over Green et al. (US Pat No. 5,583,034) taken with either Chourpa (Specgtroscopy of Bviological Molecules: Modern Trends, [European Conferenceon Spectroscopy of Biological Molecules], 7th, Madrid, 1997, 361-362 or Strode, and further in view of Matteucci (J. Am. Chem. Soc. 1997, Vol. 119, 6939-6940), and of Claims 18 and 22 under 35 USC 103(a) as being unpatentable over Chourpa (Specgtroscopy of Bviological Molecules: Modern Trends, [European Conferenceon Spectroscopy of Biological Molecules], 7th, Madrid, 1997, 361-362, taken with Matteucci (J. Am. Chem. Soc. 1997, Vol. 119, 6939-6940), have been withdrawn because applicant's response successfully argues that there is not a motivation to covalently bind a CPT to the GC based oligo, whereby the CPT can be metabolically released from the oligo.

Claims 14 and 22 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

In addition, should applicant amends the claims so as to limit the CPT-oligonucleotide complex to a CPT wherein at least a part of the CPT drug lactone ring is

associated with RNA or catalytic RNA, the claims would be free of the prior art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Dave Nguyen* whose telephone number is **(571-272-0731)**.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Amy Nelson* may be reached at **571-272-0184.**

Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is **(703) 308-0196**.

Dave Trong Nguyen
Primary Examiner
Art Unit: 1632

DAVET. NGUYEN
PRIMARY EXAMINER